

**REMARKS**

Applicants would like to thank Examiner Badeo for the courtesy extended to attorney for Applicants, Dean L. Fanelli, during a February 27, 2009 interview.

Claims 57, 70-71, 77, and 88 are currently pending in this application upon entry of this paper. Claims 1-56, 58-69, 72-76, 78-87, and 89-119 have been canceled without prejudice. Applicants reserve the right to file one or more continuation, divisional, or continuation-in-part applications directed to any withdrawn or canceled subject matter. Claim 57 has been amended to more clearly recite the claimed invention. Claims 70, 71, and 88 have been amended to remove improper dependence from canceled claims. Applicants respectfully submit that the claims have not been amended such that a new search is required. No new matter has been added by the amendments.

**I. Duplicate Claims Have Been Corrected**

Claims 60 and 72 are objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claims 56 and 57.

Applicants have canceled claims 60 and 73 without prejudice, thereby rendering the objection moot.

**II. The Claim Objections Have Been Overcome**

Claims 69, 80, and 87 are objected to under 37 C.F.R. § 1.75(c) as being improper dependent form for failing to further limit the subject matter of a previous claims.

Applicants have canceled claims 69, 80, and 87 without prejudice, thereby rendering the objection moot.

**III. The Rejections Under 35 U.S.C. § 112, First Paragraph, Should be Withdrawn**

Claims 56, 58-61, 64, 66, 69-71, and 84 are rejected on pages 3-5 of the office action under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement.

Applicants have canceled claims 56 and 58 without prejudice, thereby rendering the rejection to independent claims 56 and 58 as well as claimed dependent therefrom moot. Applicants respectfully submit that the rejection of claims 56, 58-61, 64, 66, 69-71, and 84 under 35 U.S.C. 112, first paragraph, as allegedly not enabled should be withdrawn.

**IV. The Rejection Under 35 U.S.C. § 112, Second Paragraph, Should be Withdrawn**

Claim 66 is rejected on pages 5 of the office action under 35 U.S.C. 112, second paragraph, as allegedly being indefinite.

Applicants respectfully submit that they have canceled claim 66 thereby rendering the rejection moot.

**V. The Rejection Under 35 U.S.C. § 103(a) Should be Withdrawn**

Claims 56-61, 64, 66, 69, 70-73, 77, 80-82, 84, and 87-89 are rejected on pages 3-5 of the office action under 35 U.S.C. 103(a) as allegedly obvious over U.S. patent number 5,580,899 to Mayhew *et al.* (“Mayhew”). According to the office action,

[T]he instant claims differ from the reference by reciting the corresponding 9-monounsaturated fatty acid derivative. However, Mayhew teaches both saturated and unsaturated fatty acids and C-9 monounsaturated fatty acids such as oleic acid and elaidic acid are well known in the art (reference will be provided upon request). Therefore, it would have been obvious to the skilled artisan in the art at the time of the present invention to select any of the species of the genus taught by the reference, including that of the instant claims, because an ordinary artisan would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as the genus as a whole.

(See Office action at page 6, citations to Mayhew omitted).

Applicants respectfully traverse the rejection.

The factual determinations underpinning the legal conclusion of obviousness include: (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences between the claimed invention and the prior art, and (4) evidence of secondary factors, also known as objective indicia of non-obviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). The Supreme Court reinforced this analysis in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739 (2007). The Supreme Court's analysis in *KSR* relies on several assumptions about the prior art landscape. First, *KSR* assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, *KSR* presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. *See Takeda*, 492 F.3d at 1357 ("Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound."). Third, the Supreme Court's analysis in *KSR* presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions," 127 S. Ct. at 1742. In *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008), the Federal Circuit further explained that this "easily traversed, small and finite number of alternatives . . . might support an inference of obviousness." To the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.

The pending claims encompass methods including, *inter alia*, achieving therapeutically beneficial levels of a drug in a cell. Applicants respectfully submit that the combination of references does not teach or suggest achieving therapeutically beneficial levels of a drug in a cell much less administering to a patient in need thereof a therapeutically effective amount of an anticancer drug having a covalent bond to a lipophilic moiety, wherein said lipophilic moiety is a cis- or trans-n-9 monounsaturated fatty acid having a chain length of 18 or 20 carbon atoms.

Mayhew discloses a taxane derivative comprising a hydrophobic organic moiety attached to a taxane, compositions comprising such compounds, including lipid carrier-containing compositions, and methods of administering such compositions to animals, including those afflicted with cancers. (See Mayhew at col. 1, lines 5-10). Mayhew also discloses “[h]ydrophobic organic moieties include, without limitation, saturated or unsaturated, aliphatic or branched fatty acids. Such moieties also include: polyol-, e.g., glycerol or mannitol, based amphipathic lipids comprising a polar group and one or more fatty acids.” (*Id.* at col. 5, lines 47-49).

Mayhew further discloses

at least one hydrophobic organic moiety is attached to the taxane. Furthermore, two hydrophobic organic moieties can be attached to the taxane, R then being a group having the formula  $Y^1$ ,  $Z^1X^1$  or  $Z^1D^1$  when  $R^1$  is a group having the formula  $Y^2$ ,  $Z^2X^2$  or  $Z^2D^2$ .

Each of  $Y^1$  and  $Y^2$  is independently a group having the formula:

$-C(O)(CH_2)_a(CH=CH)_b(CH_2)_c(CH=CH)_d(CH_2)_e(CH=CH)_f(CH_2)_g$   
 $(CH=CH)_h(CH_2)_i(CH_3)$ . The sum of  $a+2b+c+2d+e+2f+g+2h+i$  is equal to an integer from 7 to 22 (referring to the number of carbon atoms); a is zero or an integer from 1 to 22; each of b, d, f and h is independently zero or 1; c is zero or an integer from 1 to 20; e is zero or an integer from 1 to 17; g is zero or an integer from 1 to 14; i is zero or an integer from 1 to 11; and a to i can be the same or different at each occurrence.

(*Id.* at col. 2, lines 33-47).

Applicants respectfully submit that one of ordinary skill in the art would not have a reason to modify the known compound in a particular manner as recited by the claim to achieve therapeutically beneficial levels of a drug in a cell (*i.e.*, to include an anticancer agent covalently bonded to a *cis*- or *trans*-n-9 monounsaturated fatty acid having a chain length of 18 or 20 carbon atoms) to establish *prima facie* obviousness for the claimed methods. See *Takeda*, 492 F.3d at 1357. Indeed, the “two hydrophobic organic moieties attached to the taxane” disclosed by Mayhew literally include millions of hydrophobic organic moieties. Even Mayhew’s disclosure

“[m]ore preferably, each of Y<sup>1</sup> and Y<sup>2</sup> is independently -C(O)(CH<sub>2</sub>)<sub>10</sub>CH<sub>3</sub> or --C(O)(CH<sub>2</sub>)<sub>16</sub>CH<sub>3</sub> does not amount to a legally required prima facie case of obviousness. Indeed, the Federal Circuit explained that an “easily traversed, small and finite number of alternatives . . . might support an inference of obviousness.” However, to the extent an art is unpredictable, as the chemical arts often are, *KSR*’s focus on these “identified, predictable solutions” *may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.* (See *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008); *Applicants’ emphasis*).

Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness. The necessary “structural similarity between claimed and prior art subject matter . . . where the prior art gives reason or motivation to make the claimed compositions required to establish a *prima facie* case of obviousness” is absent. See *Eisai Co. v. Dr. Reddy’s Laboratories, Ltd.* 533 F.3d 1353 (Fed. Cir. 2008) and *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, 1377 (Fed. Cir. 2006) (*quoting In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (*en banc*))).

For at least the above reasons, Applicants respectfully submit that the rejection of Claims 57, 70-71, 77, and 88 under 35 U.S.C. 103(a) as allegedly obvious over Mayhew should be reconsidered and withdrawn.

## **VI. Conclusions**

Should the Examiner disagree with any of the above arguments, Applicants respectfully request a telephone interview with the Examiner and undersigned attorney for Applicants to advance the prosecution of the application.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a Constructive Petition for Extension of Time in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

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/Dean L. Fanelli/  
Dean L. Fanelli (Reg. No. 48,907)

**MORGAN, LEWIS & BOCKIUS LLP**

**Customer No.: 009629**

1111 Pennsylvania Avenue, N.W.  
Washington, D.C. 20004  
(202) 739-3000-phone  
(202) 739-3001-fax